AMENDMENTS TO THE SPECIFICATION

Please amend the title of the application on page 1 to read as follows:

ANTIBODY THAT BINDS ~~NUCLEIC ACID AND ENCODED~~ ZINC TRANSPORTER PROTEIN ~~ENTITLED~~ 108P5H8 ~~USEFUL IN TREATMENT AND DETECTION OF CANCER~~

Please amend the specification at page 6, lines 27-38 as follows:

Figure 1. The 108P5H8 sequence of 448 nucleotides (SEQ ID NO: 2568).

Figure 2. The cDNA (SEQ ID. NO. : 2569) and amino acid sequence (SEQ ID. NO. : 2570) of 108P5H8 v.1 is shown in Figure 2A. The start methionine is underlined. The open reading frame extends from nucleic acid 253-1542 including the stop codon. The nucleic acid (SEQ ID. NO. : 2571) and amino acid sequence of 108P5H8 variant 2 (SEQ ID. NO. : 2572) is shown in Figure 2B, the codon for the start methionine is underlined. The open reading frame for variant 2 extends from nucleic acid 1 to 1290 including the stop codon. The nucleic acid (SEQ ID. NO. : 2573) and amino acid sequence of 108P5H8 variant 3 (SEQ ID. NO. : 2574) is shown in Figure 2C, the codon for the start methionine is underlined. The open reading frame for variant 3 extends from nucleic acid 1-1290 including the stop codon.

Figure 3. Amino acid sequence of 108P5H8 variant 1 and of 108P5H8 variant 2 (SEQ ID. NO. : 2572) is shown in Figure 3A. The proteins encoded by the variant 1 and variant 2 nucleic acid sequences are identical and each have 429 amino acids. The amino acid sequence of 108P5H8 variant 3 (SEQ ID. NO. : 2574) is shown in Figure 3B, the 108P5H8 v.3 protein has 429 amino acids.

Please amend the specification at page 7, lines 1-20 as follows:

Figure 4. 4A shows nucleotide sequence alignments of 108P5H8 variants 1-3 and 4B shows amino ~~Amino~~ acid alignments of 108P5H8 ~~variants 1-3~~ variant 1 (SEQ ID. NO. : 2570), variant 2 (SEQ ID. NO. : 2572) and variant 3 (SEQ ID. NO. : 2574).

Figure 5. Hydrophilicity amino acid profile of 108P5H8 determined by computer algorithm sequence analysis using the method of Hopp and Woods (Hopp T.P., Woods K.R., 1981. Proc. Natl.

Acad. Sci. U.S.A. 78:3824-3828) accessed on the Protscale website ~~(www.expasy.ch/cgi-bin/protscale.pl)~~ through the ExPasy molecular biology server.

Figure 6. Hydropathicity amino acid profile of 108P5H8 determined by computer algorithm sequence analysis using the method of Kyte and Doolittle (Kyte J., Doolittle R.F., 1982. J. Mol. Biol. 157:105-132) accessed on the ProtScale website ~~(www.expasy.ch/cgi-bin/protscale.pl)~~ through the ExPasy molecular biology server.

Figure 7. Percent accessible residues amino acid profile of 108P5H8 determined by computer algorithm sequence analysis using the method of Janin (Janin J., 1979 Nature 277:491-492) accessed on the ProtScale website ~~(www.expasy.ch/cgi-bin/protscale.pl)~~ through the ExPasy molecular biology server.

Figure 8. Average flexibility amino acid profile of 108P5H8 determined by computer algorithm sequence analysis using the method of Bhaskaran and Ponnuswamy (Bhaskaran R., and Ponnuswamy P.K., 1988. Int. J. Pept. Protein Res. 32:242-255) accessed on the ProtScale website ~~(www.expasy.ch/cgi-bin/protscale.pl)~~ through the ExPasy molecular biology server.

Figure 9. Beta-turn amino acid profile of 108P5H8 determined by computer algorithm sequence analysis using the method of Deleage and Roux (Deleage, G., Roux B. 1987 Protein Engineering 1:289-294) accessed on the ProtScale website ~~(www.expasy.ch/cgi-bin/protscale.pl)~~ through the ExPasy molecular biology server.

Please amend the specification at page 9, lines 3-20 as follows:

Figure 18. Secondary structure and transmembrane prediction for 108P5H8 (SEQ ID. NO. : 2570). The secondary structure of 108P5H8 protein was predicted using the HNN - Hierarchical Neural Network method (Guermeur, 1997~~, http://pbil.ibcp.fr/cgi-bin/npsa_automat.pl?page=npsa_nn.html~~), accessed from the ExPasy molecular biology server ~~(http://www.expasy.ch/tools/)~~. This method predicts the presence and location of alpha helices, extended strands, and random coils from the primary protein ~~sequence~~ sequence. The percent of the protein in a given secondary structure is also given.

Figure 19. Transmembrane prediction for 108P5H8. A. Schematic representation of the probability of existence of transmembrane regions and orientation of 108P5H8 based on the

TMpred algorithm of Hofmann and Stoffel which utilizes TMBASE (K. Hofmann, W. Stoffel. TMBASE - A database of membrane spanning protein segments Biol. Chem. Hoppe-Seyler 374:166, 1993). B. Schematic representation of the probability of the existence of transmembrane regions and the extracellular and intracellular orientation of 108P5H8 based on the TMHMM algorithm of Sonnhammer, von Heijne, and Krogh (Erik L.L. Sonnhammer, Gunnar von Heijne, and Anders Krogh: A hidden Markov model for predicting transmembrane helices in protein sequences. In Proc. of Sixth Int. Conf. on Intelligent Systems for Molecular Biology, p 175-182 Ed J. Glasgow, T. Littlejohn, F. Major, R. Lathrop, D. Sankoff, and C. Sensen Menlo Park, CA: AAAI Press, 1998). The TMpred and TMHMM algorithms are accessed from the ExPasy molecular biology server ~~(http://www.expasy.ch/tools/)~~. The results of the transmembrane prediction programs presented in A and B depict 108P5H8 as containing 6 transmembrane domains.

Please amend the specification at page 10, line 16 as follows:

Figure 25. 25A shows an alignment of 108P5H8 protein (SEQ ID. NO. : 2570)~~variants show homology to~~ with the human zinc transporter 4, i.e. gi 11432533 (SEQ ID. NO. : 2579); 25B shows an alignment of 108P5H8 protein with the human zinc transporter ZNT4, i.e. gi 8134840 (SEQ ID. NO. : 2580); and 25C shows an alignment of 108P5H8 protein with the rat zinc transporter ZNT-4, i.e. gi 8134837 (SEQ ID. NO. : ?);.

Please amend the specification at page 24, lines 9-15 as follows:

As discussed herein, redundancy in the genetic code permits variation in 108P5H8 gene sequences. In particular, it is known in the art that specific host species often have specific codon preferences, and thus one can adapt the disclosed sequence as preferred for a desired host. For example, preferred analog codon sequences typically have rare codons (i.e., codons having a usage frequency of less than about 20% in known sequences of the desired host) replaced with higher frequency codons. Codon preferences for a specific species are calculated, for example, by utilizing codon usage tables available on the INTERNET ~~such as at URL www.dna.affrc.go.jp/~nakamura/codon.html~~.

Please amend the specification at page 27, lines 11-24 as follows:

Additional illustrative embodiments of the invention disclosed herein include 108P5H8 polypeptides comprising the amino acid residues of one or more of the biological motifs contained within a 108P5H8 polypeptide sequence set forth in Figure 2 or Figure 3. Various motifs are known in the art, and a protein can be evaluated for the presence of such motifs by a number of publicly available Internet sites (see, e.g., ~~URL addresses: pfam.wustl.edu/; http://searchlauncher.bcm.tmc.edu/seq-search/struc-predict.html; psort.ims.u-tokyo.ac.jp/; www.cbs.dtu.dk/; www.ebi.ac.uk/interpro/scan.html; www.expasy.ch/tools/scnpsit1.html;~~ Epimatrix™ and Epimer™, Brown University, ~~www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html~~; and BIMAS~~, bimas.dcrt.nih.gov/.~~).

Motif bearing subsequences of all 108P5H8 variant proteins are set forth and identified in Table XIX.

Table XX sets forth several frequently occurring motifs based on pfam searches ~~(see URL address pfam.wustl.edu/)~~. The columns of Table XX list (1) motif name abbreviation, (2) percent identity found amongst the different member of the motif family, (3) motif name or description and (4) most common function; location information is included if the motif is relevant for location.

Please amend the specification at page 28, lines 1-10 as follows:

In another embodiment, proteins of the invention comprise one or more of the immunoreactive epitopes identified in accordance with art-accepted methods, such as the peptides set forth in Tables V-XVIII, XXII, and XXIII. CTL epitopes can be determined using specific algorithms to identify peptides within an 108P5H8 protein that are capable of optimally binding to specified HLA alleles (e.g., Table IV; Epimatrix™ and Epimer™, Brown University, ~~URL www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html;~~ and BIMAS~~, URL bimas.dcrt.nih.gov/.~~) Moreover, processes for identifying peptides that have sufficient binding affinity for HLA molecules and which are correlated with being immunogenic epitopes, are well known in the art, and are carried out without undue experimentation. In addition, processes for identifying peptides that are immunogenic epitopes, are well known in the art, and are carried out without undue experimentation either *in vitro* or *in vivo*.

Please amend the specification at page 29, lines 20-31 as follows:

CTL epitopes can be determined using specific algorithms to identify peptides within an 108P5H8 protein that are capable of optimally binding to specified HLA alleles (e.g., by using the SYFPEITHI site at World Wide Web ~~URL syfpeithi.bmi-heidelberg.com/~~; the listings in Table IV(A)-(E); Epimatrix™ and Epimer™, Brown University~~, URL (www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html);~~ and BIMAS~~, URL bimas.dcrt.nih.gov/~~). Illustrating this, peptide epitopes from 108P5H8 that are presented in the context of human MHC class I molecules HLA-A1, A2, A3, A11, A24, B7 and B35 were predicted (Tables V-XVIII, XXII, and XXIII). Specifically, the complete amino acid sequence of the 108P5H8 protein and relevant portions of other variants, i.e., for HLA Class I predictions 9 flanking residues ~~redisues~~ on either side of a point mutation, and for HLA Class II predictions14 flanking residues on either side of a point mutation, were entered into the HLA Peptide Motif Search algorithm found in the Bioinformatics and Molecular Analysis Section (BIMAS) web site listed above; for HLA Class II the site SYFPEITHI ~~at URL syfpeithi.bmi-heidelberg.com/~~ was used.

Please amend the specification at the paragraph bridging pages 47 and 48 as follows:

CTL epitopes can be determined using specific algorithms to identify peptides within 108P5H8 protein that bind corresponding HLA alleles (see e.g., Table IV; Epimer™ and Epimatrix™, Brown University ~~(URL www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html)~~; and, BIMAS, ~~(URL bimas.dcrt.nih.gov/; SYFPEITHI at URL syfpeithi.bmi-heidelberg.com/)~~. In a preferred embodiment, a 108P5H8 immunogen contains one or more amino acid sequences identified using techniques well known in the art, such as the sequences shown in Tables V-XVIII, XXII, and XXIII or a peptide of 8, 9, 10 or 11 amino acids specified by an HLA Class I motif/supermotif (e.g., Table IV (A), Table IV (D), or Table IV (E)) and/or a peptide of at least 9 amino acids that comprises an HLA Class II motif/supermotif (e.g., Table IV (B) or Table IV (C)). As is appreciated in the art, the HLA Class I binding groove is essentially closed ended so that peptides of only a particular size range can fit into the groove and be bound, generally HLA Class I epitopes are 8, 9, 10, or 11 amino acids long. In contrast, the HLA Class II binding groove is essentially open ended; therefore a peptide of about 9 or more amino acids can be bound by an HLA Class II molecule. Due to the

binding groove differences between HLA Class I and II, HLA Class I motifs are length specific, i.e., position two of a Class I motif is the second amino acid in an amino to carboxyl direction of the peptide. The amino acid positions in a Class II motif are relative only to each other, not the overall peptide, i.e., additional amino acids can be attached to the amino and/or carboxyl termini of a motif-bearing sequence. HLA Class II epitopes are often 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids long, or longer than 25 amino acids.

Please amend the specification at the paragraph bridging pages 48 and 49 as follows:

Vaccine compositions of the invention include nucleic acid-mediated modalities. DNA or RNA that encode protein(s) of the invention can be administered to a patient. Genetic immunization methods can be employed to generate prophylactic or therapeutic humoral and cellular immune responses directed against cancer cells expressing 108P5H8. Constructs comprising DNA encoding a 108P5H8-related protein/immunogen and appropriate regulatory sequences can be injected directly into muscle or skin of an individual, such that the cells of the muscle or skin take-up the construct and express the encoded 108P5H8 protein/immunogen. Alternatively, a vaccine comprises a 108P5H8-related protein. Expression of the 108P5H8-related protein immunogen results in the generation of prophylactic or therapeutic humoral and cellular immunity against cells that bear a 108P5H8 protein. Various prophylactic and therapeutic genetic immunization techniques known in the art can be used ~~(for review, see information and references published at Internet address www.genweb.com)~~. Nucleic acid-based delivery is described, for instance, in Wolff *et. al.*, *Science* 247:1465 (1990) as well as U.S. Patent Nos. 5,580,859; 5,589,466; 5,804,566; 5,739,118; 5,736,524; 5,679,647; WO 98/04720. Examples of DNA-based delivery technologies include "naked DNA", facilitated (bupivicaine, polymers, peptide-mediated) delivery, cationic lipid complexes, and particle-mediated ("gene gun") or pressure-mediated delivery (*see, e.g.*, U.S. Patent No. 5,922,687).

Please amend the specification at page 76, lines 31-32 as follows:

This mapping vector and the mapping program ~~at http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl~~ placed 108P5H8 to chromosome 15q15.2-q21.1.

Please amend the specification at page 83, lines 16-18 as follows:

Figure 5, Figure 6, Figure 7, Figure 8, and Figure 9 depict graphically five amino acid profiles of the 108P5H8 amino acid sequence (variant 1), each assessment is available by accessing the ProtScale website ~~(URL www.expasy.ch/cgi-bin/protscale.pl)~~ on the ExPasy molecular biology server.

Please amend the specification at page 84, lines 19-31 as follows:

The secondary structure of 108P5H8, namely the predicted presence and location of alpha helices, extended strands, and random coils, is predicted from the primary amino acid sequence of 108P5H8 variant 1 using the HNN - Hierarchical Neural Network method (Guermeur, 1997~~;~~ ~~http://pbil.ibcp.fr/cgi-bin/npsa_automat.pl?page=npsa_nn.html~~), accessed from the ExPasy molecular biology server ~~(http://www.expasy.ch/tools/)~~. The analysis indicates that 108P5H8 is composed of 49.88% alpha helix, 11.66% extended strand, and 38.46% random coil (Figure 18).

Analysis for the potential presence of transmembrane domains in 108P5H8 was carried out using a variety of transmembrane prediction algorithms accessed from the ExPasy molecular biology server ~~((http://www.expasy.ch/tools/)~~. The programs predict the presence of 6 transmembrane domains in 108P5H8. Shown graphically in Figure 19A and19B are the results of analysis using the TMpred and TMHMM prediction programs, respectively, depicting the location of the 6 transmembrane domains. The results of each program, namely the amino acids encoding the transmembrane domains are summarized in Table XXI.

Please amend the specification at page 113, lines 20-29 as follows:

Antibody efficacy on tumor growth and metastasis formation is studied, e.g., in mouse subcutaneous or orthotopic prostate cancer xenograft models and mouse kidney xenograft models. The antibodies can be unconjugated, as discussed in this Example, or can be conjugated to a therapeutic modality, as appreciated in the art. Anti-108P5H8 mAbs inhibit formation of both the androgen-dependent LAPC-9 and androgen-independent PC3-108P5H8 tumor xenografts. Anti-108P5H8 mAbs also retard the growth of established orthotopic tumors and prolonged survival of tumor-bearing mice. These results indicate the utility of anti-108P5H8 mAbs in the treatment of

local and advanced stages of, e.g., prostate cancer. (See, e.g., Saffran, D., *et al.*, PNAS 10:1073-1078 ~~or www.pnas.org/cgi/doi/10.1073/pnas.051624698~~). These results indicate the use of anti-108P5H8 mAbs in the treatment of prostate cancer.

Please amend the paragraph bridging pages 114 and 115 of the specification as follows:

Subcutaneous (s.c.) tumors are generated by injection of 1 x 10^6 LAPC-9, PC3, PC3-108P5H8, DU145 or DU145-108P5H8 cells mixed at a 1:1 dilution with Matrigel (Collaborative Research) in the right flank of male SCID mice. To test antibody efficacy on tumor formation, i.p. antibody injections are started on the same day as tumor-cell injections. As a control, mice are injected with either purified mouse IgG (ICN) or PBS; or a purified monoclonal antibody that recognizes an irrelevant antigen not expressed in human cells. In preliminary studies, no difference is found between mouse IgG or PBS on tumor growth. Tumor sizes are determined by vernier caliper measurements, and the tumor volume is calculated as length x width x height. Mice with s.c. tumors greater than 1.5 cm in diameter are sacrificed. PSA levels are determined by using a PSA ELISA kit (Anogen, Mississauga, Ontario). Circulating levels of anti-108P5H8 mAbs are determined by a capture ELISA kit (Bethyl Laboratories, Montgomery, TX). (See, e.g., (Saffran, D., *et al.*, PNAS 10:1073-1078 ~~or www.pnas.org/cgi/ doi/10.1073/pnas.051624698~~).

Please amend the specification at page 128, lines 2-4 as follows:

Adapted from the GCG Software 9.0 BLOSUM62 amino acid substitution matrix (block substitution matrix). The higher the value, the more likely a substitution is found in related, natural proteins. ~~(See URL www.ikp.unibe.ch/manual/blosum62.html)~~

Please amend the specification at page 166, as follows:

TABLE XXI: Properties of 108P5H8

Motifs and localization apply to 108P5H8 variants 1 and 2.

	Bioinformatic Program	~~URL~~	Outcome
ORF	ORF Finder	~~http://www.ncbi.nlm.gov/gorf~~	1290

			(includes stop)
Protein Length	n/a	~~n/a~~	429 amino acids
Transmembrane region	TM Pred	~~http://www.ch.embnet.org/~~	6 TM, at amino acids 114-130, 147-163, 181-200, 217-236, 273-295, 306-324
	HMMTop	~~http://www.enzim.hu/hmmtop/~~	6 TM, at amino acid 113-130, 135-164, 179-202, 215-236, 271-296, 306-331
	Sosui	~~http://www.genome.ad.jp/SOSui/~~	6 TM, at amino acid 113-135, 141-163, 180-202, 215-237, 272-294, 308-330
	TMHMM	~~http://www.cbs.dtu.dk/services/TMHMM~~	6 TM, at amino acids 114-136, 146-165, 178-200, 215-237, 273-295, 310-332
Signal Peptide	Signal P	~~http://www.cbs.dtu.dk/services/SignalP/~~	indicates no signal
pI	pI/MW tool	~~http://www.expasy.ch/tools/~~	pI 6.11
Molecular weight	pI/MW tool	~~http://www.expasy.ch/tools/~~	47.5 kDa
Localization	PSORT	~~http://psort.nibb.ac.jp/~~	Plasma membrane 60%
	PSORT II	~~http://psort.nibb.ac.jp/~~	Plasma membrane 43%
	iPSORT	~~http://psort.nibb.ac.jp~~	No signal motif
Motifs	Pfam	~~http://www.sanger.ac.uk/Pfam/~~	Ribosomal protein L34; Cation efflux family
	Prints	~~http://www.biochem.ucl.ac.uk/~~	Rhodopsin
	Blocks	~~http://www.blocks.fhcrc.org/~~	No motif
	Prosite	~~http://www.genome.ad.jp/~~	No motif